CLAIMS

WHAT IS CLAIMED IS:

1. A synthetic derivative of an original polyamine, wherein a carbon atom of said original polyamine comprises an amide group, said synthetic derivative inhibiting the cellular uptake of a natural polyamine by specifically binding a cellular transporter for said natural polyamine.

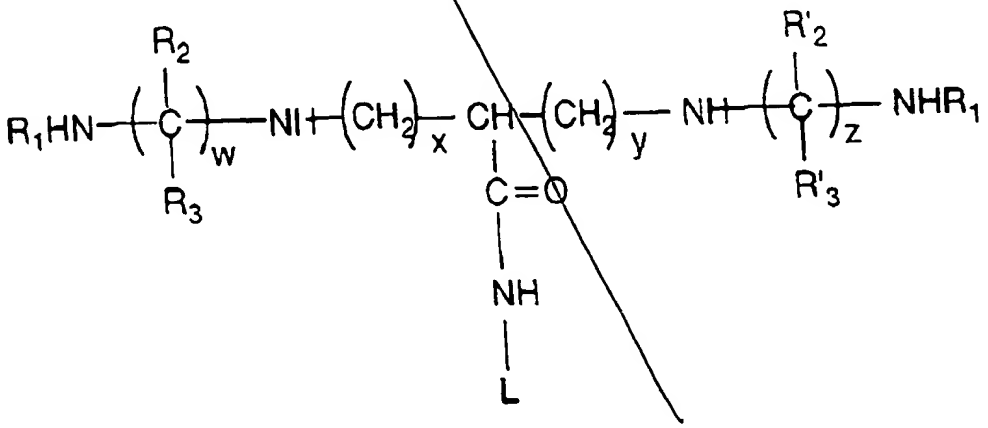
2. A synthetic derivative according to claim 1, wherein the carbon to which said amido group is located between two internal nitrogen atoms of said original polyamine.

3. A synthetic derivative according to claim 2 which comprises a dimer of said original polyamine, the monomers of said dimer being liked together by a spacer side chain anchored to the amido group of each monomer.

4. A synthetic derivative according to claim 3, wherein the original polyamine is selected from the group consisting of putrescine, spermidine and spermine.

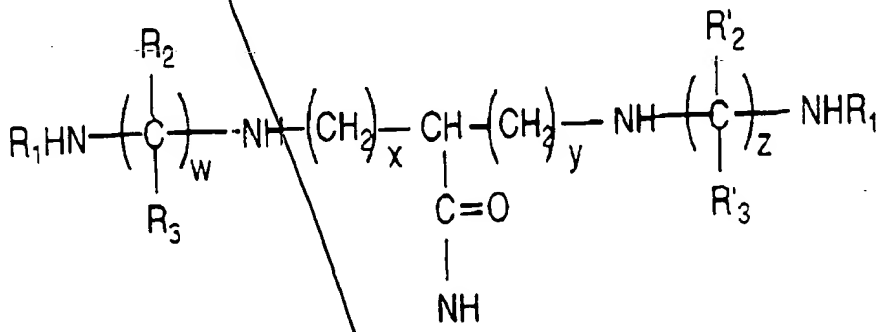
5. A synthetic derivative according to claim 4, wherein the original polyamine is spermine.

6. A synthetic derivative according to claim 2, wherein said synthetic derivative has the following general formula:



in which R_1 and R'_1 independently represent a hydrogen atom or an alkyl group having 1 to 3 carbon atoms, R_2, R'_2, or R_3 and R'_3 independently represent a hydrogen atom or a methyl group, w and z independently represent an integer of 3 or 4, x represents an integer from 0 to n, y represents an integer from 0 to n, n represents an integer from 3 to 6, the sum of x and y equals n, and L represents a hydrogen atom or a molecule which cannot be captured by said natural polyamine transporter.

7. A synthetic derivative according to claim 3, wherein said monomer has the following general formula:



in which R_1 and R'_1 independently represent a hydrogen atom or an alkyl group having 1 to 3 carbon atoms, R_2, R'_2, or R_3 and R'_3 independently represent a hydrogen atom or a methyl group, w and z independently represent an integer of 3 or 4, x represents an integer from 0 to n, y represents an integer from 0 to n, n represents an integer from 3 to 6, the sum of x and y equals n, and L is the spacer side chain that comprises a linear hydrocarbon-containing backbone of 3 to 8 atoms.

8. A derivative according to claim 7, wherein said backbone comprises sulfur, oxygen, phosphorus or nitrogen.

9. A derivative according to claim 8, wherein w=3, z=3, x=0 and y=3.

10. A derivative according to claim 7, wherein w=3, z=3, x=0 and y=3

11. A derivative according to claim 8, wherein w=3, z=3, x=0 and y=4

12. A derivative according to claim 9, wherein the hydrocarbon-containing backbone comprises a disulfide bridge.

13. A derivative according to claim 9, which is *N*(2-mercaptoethyl)spermine-5-carboxamide.

14. A derivative according to claim 9, which is *N*(2,2'-dithio(ethyl, 1'-aminoethyl)spermine-5-carboxamide.

15. A derivative according to claim 12 which is 2,2'-dithiobis(*N*-ethylspermine-5-carboxamide).

16. The use of a synthetic derivative according to any one of claims 1 to 15 for inhibiting the activity of a natural polyamine transporter comprising the step of contacting said transporter with an inhibitory effective amount of said synthetic derivative.

17. The use according to claim 16, which results in the control or the treatment of disorders involving unrestrained cell proliferation and/or differentiation where control of polyamine transport is required, when used in combination with an inhibitor of polyamine synthesis.

18. The use according to claim 16, wherein the inhibitor of a polyamine synthesis is DFMO.

19. The use of the synthetic derivative of any one of claims 1, 2, 6, 9, 13 and 14 as a marker for a polyamine transporter, wherein said synthetic derivative comprises a detectable label having affinity for a polyamine transporter and wherein said use comprises the steps of labeling said synthetic derivative to provide a labeled synthetic derivative, binding said labeled synthetic derivative to a polyamine transporter, and employing said labeled synthetic derivative bound to a polyamine transporter as a marker for the detection of a polyamine transporter.

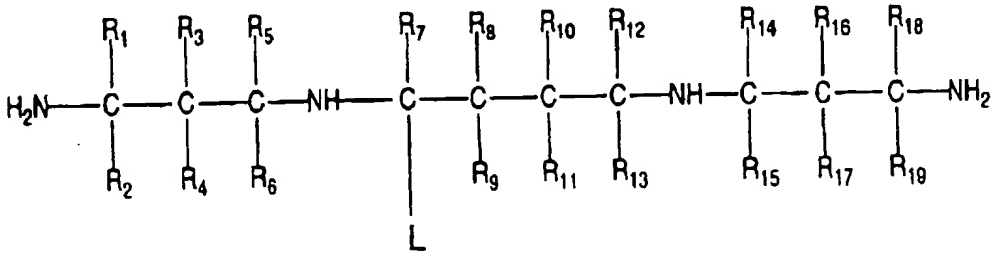
20. The use according to claim 19 which results in the diagnosis of a disorder involving unrestrained cell proliferation and/or differentiation where control of polyamine transport is required.

21. A pharmaceutical composition for treating disorders wherein control of polyamine transport is required, comprising a synthetic derivative according to any one of claims 1 to 15 in combination with an acceptable pharmaceutical carrier.

22. A pharmaceutical composition according to claim 21, which further comprises an inhibitor of polyamine synthesis.

23. A pharmaceutical composition according to claim 22, wherein said inhibitor of polyamine synthesis is a α-difluoromethylornithine.

24. A synthetic derivative of a polyamine comprising

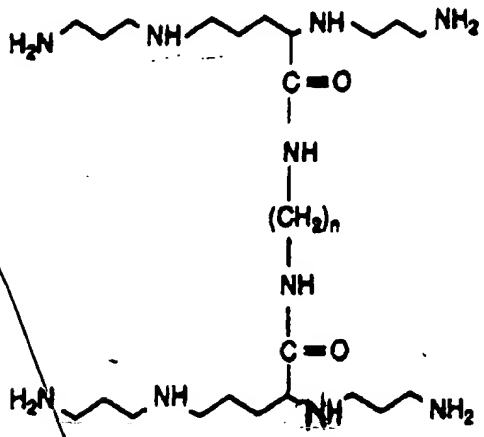


wherein R_1 or R_2 and R_{18} or R_{19} is methyl, R_3 through R_{17} is H or methyl, and L is a linker comprising a chemical entity covalently attached to said polyamine and capable of modifying the membrane permeability of a polyamine analog.

25. The derivative of claim 24 wherein the L is a α,ω-diamine cross-linker.

26. The synthetic derivative of Claim 25 wherein at least one of R_1 and R_2 and one of R_{18} and R_{19} are methyl groups.

27. A synthetic derivative of a polyamine having a structure:



wherein n is 3, 4, 5 or 6.

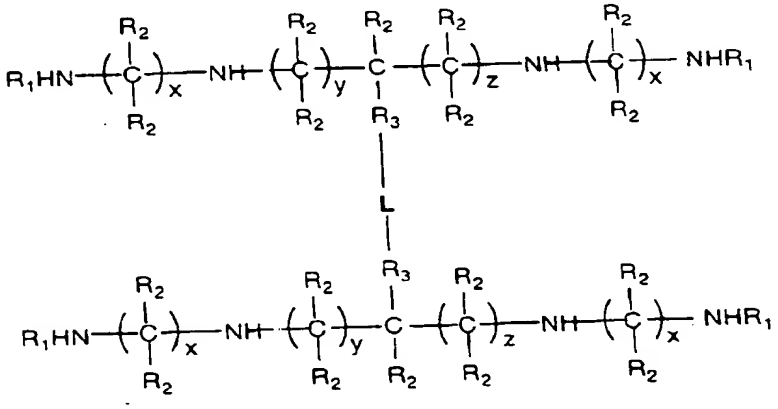
28. The synthetic derivative of claim 27 wherein n is 3.

29. The synthetic derivative of claim 27 wherein n is 4.

30. The synthetic derivative of claim 27 wherein n is 5.

31. The synthetic derivative of claim 27 wherein n is 6.

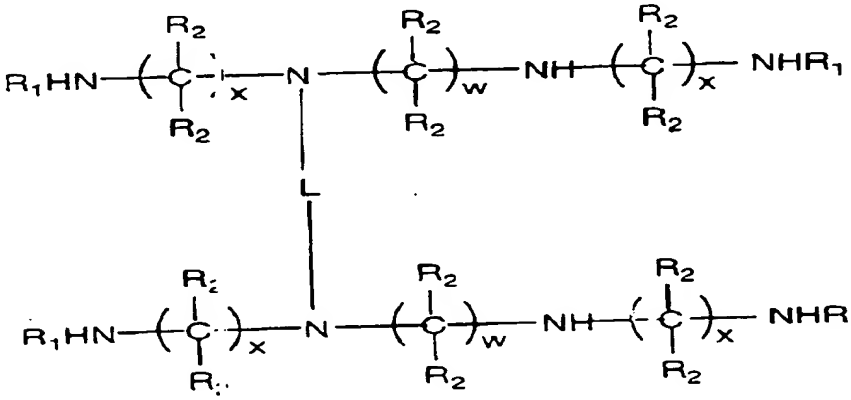
32. A synthetic derivative of a polyamine comprising Structure 1:



wherein R_1 is H, methyl, ethyl or propyl, R_2 is H or methyl, x is greater than two and less than five ($2<x<5$), and the sum of y+z is greater than or equal to 6 ($2 \leq y + z \leq 6$), R_3 is an alkyl, amide, keto, ether. thioether, phosphono or sulfonyl group: and L is a linker as defined in claim 24.

33. The synthetic derivative of claim 32 wherein x is 3, R_1 is hydrogen, R_2 is a methyl (CH_3) group for the carbon atom located next to each NH-R_1 group, and is a hydrogen atom for all other carbons, y + Z = 3, and L is $-CH_2-HN(CH_2)_nNH-CH_2-$, where n = 3, 4, 5 or 6.

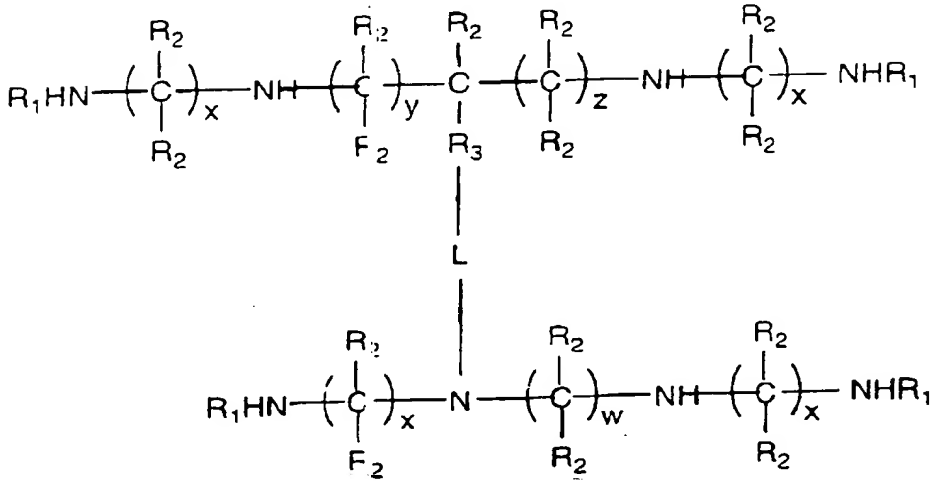
34. A synthetic derivative of a polyamine comprising Structure 2:



wherein R_1 is H, methyl, ethyl or propyl, R_2 is H or methyl, x is greater than two and less than five ($2<x<5$), w is greater than 2 and less than 8 ($2<w<8$) and L is a linker as defined in claim 24.

35. The synthetic derivative of claim 34 wherein x=3, R_1 is a hydrogen atom, R_2 is a methyl (CH_3) group for the carbon atom located next to each NH-R_1 group, and is a hydrogen atom for all other carbons and w = 4.

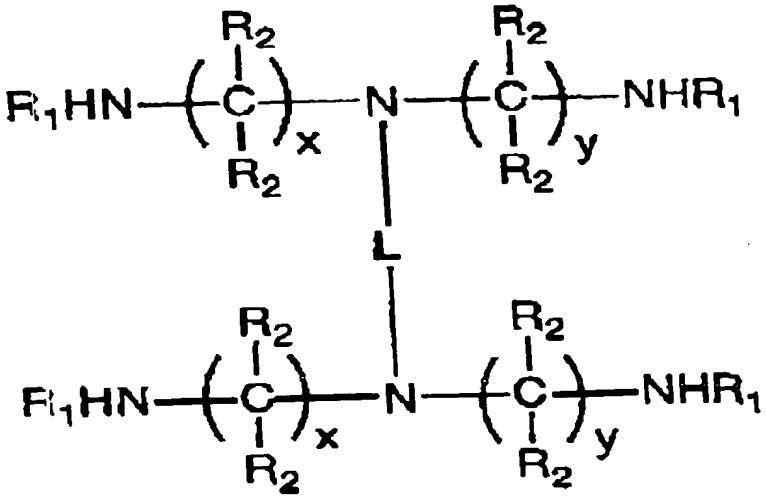
36. A synthetic derivative of a polyamine comprising Structure 3:



wherein R_1 is H, methyl, ethyl or propyl, R_2 is H or methyl, x is greater than two and less than five ($2<x<5$), w is greater than 2 and less than 8 ($2<w<8$), and R_3 is an alkyl, amide, keto, ether, thioether, phosphono or sulfonyl group; the sum of y+z is greater than or equal to 2 and less than or equal to 6 ($2 \leq y + z \leq 6$); and L is a linker as defined in claim 24.

37. The synthetic derivative of claim 35 wherein L is an aliphatic chain with a length of 2 to about 14 carbon atoms.

38. A synthetic derivative comprising a structure of a first polyamine chain and a second polyamine chain having a structure:



wherein R_1 is H, methyl , ethyl or propyl, R_2 is H or methyl, x is greater than 2 and less than 5, y is greater than 2 and less than 5, and L is a chemical linker covalently connecting said first polyamine chain to said second polyamine chain.

39. The sythetic derivative of claim 38, wherein the chemical liker is a α, ω, - diamine cross-linker.

40. The synthetic derivative of claim 38 wherein the chemical linker is further defined as an alkyl chemical linker.

41. The synthetic derivative of claim 38, when R_1 is H, X is 3 or 4, Y is 3 or 4, andf X + Y is greater than 5 and less than 9.

42. The synthetic derivative of claim 38 wherein L is an aliphatic carbon chain having a structure C- (CH_2) η, and η is greater than 2 and less than 10.

43. The synthetic derivative of claim 38 when L is xylene.